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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,490	04/06/2001	Elizabeth S. Stuart	08952-008001 / UMA 00-19	5744

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,490	STUART ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9,10 and 18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9,10 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/04, 10/04, 2/06*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *11/4/2005*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is responsive to Applicant's response filed on November 21, 2005. Claims 1-6 and 11-17 have been cancelled. Upon further review and consideration the finality of the last Office action has been withdrawn. A Non-Final Office action is set forth below.

Rejections Withdrawn

2. In view of Applicant's amendment and response the following rejections are withdrawn:

a) Rejection of claims 7, 9 and 18-20 under 35 U.S.C. 103(a), pages 2-7, paragraph 4.

b) Rejection of claim 10 under 35 U.S.C. 103(a), pages 7-9, paragraph 5.

c) Rejection of claim 10 under 35 U.S.C. 103(a), pages 9-12, paragraph 6.

d) Rejection of claim 18 under 35 U.S.C. 112, second paragraph, page 12, paragraph 8 (not withdrawn in Final Action mailed 4/19/2005).

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 7, 9 and 18-20 are rejected under 35 U.S.C. 103(a) unpatentable over in view of Whittum-Hudson et al *(Nature Medicine, Volume 2, Number 10, October 1996)* in view of Stuart et al *(Immunology, 1987)* in view of Stuart et al *(Current Microbiology, Vol. 28, 1994, pp. 85-90)* and in further view of Dick, Jr. et al *(Conjugate Vaccine, Contrib. Microbiol Immunolo. Basel., Karger 1989, Vol. 10, pp. 48-114).*

Claims 7, 9 and 18-20 are drawn to a composition comprising a carrier group coupled to one or more isolated oligosaccharides that are cleaved from or are chemically synthesized to correspond to oligosaccharides cleaved form, a chlamydial glycolipid exoantigen (GLXA).

Whittum-Hudson et al teach that the chlamydial exoglycolipid antigen (GLXA) is expressed at all differentiation stages of the *Chlamydia* organism and is secreted from infected cells (page 1116, 2nd column). Whittum-Hudson et al teach that antigenic

determinants of GLXA reside on its polysaccharide component (GLXA oligosaccharide) (page 1116).

Whittum-Hudson et al teach do not an isolated GLXA oligosaccharide.

Stuart et al, 1987 teach an isolated polysaccharide component (GLXA oligosaccharide) (pages 527-530). Stuart et al, 1987 teach that the polysaccharide component is antigenic (page 527).

Stuart et al, 1987 do not teach that the monoclonal antibody 89MS30.

Stuart et al, 1994, teach that the epitope on the polysaccharide component is recognized and binds to the monoclonal antibody 89MS30 (page 89).

Whitten-Hudson et al, Stuart et al, 1987 and Stuart et al, 1994 do not teach that the GLXA oligosaccharide is coupled to a carrier molecule.

Dick, Jr. et al teach conjugation of bacterial carbohydrate (polysaccharide) antigens to a carrier protein. Dick, Jr. et al teach that some subjects (e.g. children under 18 months and elderly people) fail to produce antibodies when stimulated with capsular polysaccharide immunogens (CPS) at level too low to be protective (page 49). Dick, Jr. et al teach that high-risk populations retain the ability to produce protective antibodies against immunogenic proteins such as diphtheria toxoid or tetanus toxoid by a process that can be adapted to carbohydrate antigens (page 49). Dick, Jr. et al teach that proteins and polysaccharides are classified into two separate classes of antigens thymus dependent (TD) and thymus independent (TI) antigens, respectively (page 49). Dick et al teach that polysaccharides classified as TI antigens have multiple repeat epitopes on their polymeric chains which collectively bind and cross-link immunoglobulin

receptors on the surface of B cells and the net effect is the induction of cellular differentiation processes that yield antibody-producing plasma cells (page 49). Dick, Jr. et al teach that it is well established that covalent bonding of carbohydrate antigens to proteins can transform the carbohydrate into the status of a TD antigen (pages 49 and 56). Dick, Jr. et al teach that CPS can be linked to carrier proteins directly or by bifunctional linkers (spacer arms) (pages 71-72) which overcome conjugation limitations imposed by steric effects (page 71). Dick, Jr. et al teach that linkers can promote improved antigenicity for the bound components as compared to results obtained when testing the same antigens conjugated by a direct method (page 72). Dick, Jr. et al teach that spacers (i.e. linkers) permit corresponding increases in translational and rotational characteristics of the antigens, increasing access of the binding sites to soluble antigens (page 72). Dick, Jr. et al teach that linkers can be covalently bound to carbohydrate components (page 70).

It would be *prima facie* obvious at the time the invention was made to covalently couple the oligosaccharide/polysaccharide from chlamydial GLXA as taught by the combined prior art references (Whittum-Hudson et al, Stuart et al, 1987 and Stuart et al, 1994) to a carrier protein (e.g. diphtheria toxoid or tetanus toxoid) as taught by Dick, Jr. et al because Stuart et al, 1987 teach that GLXA polysaccharide is antigenic and Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins thereby, demonstrating a thymus dependent (TD) response to carbohydrate components and enhancing the immune response to carbohydrate component. It would be expected barring evidence to the contrary, a composition comprising GLXA

covalently coupled to a carrier protein would be effective in stimulating a response from the immune system since the polysaccharide component has been demonstrated to be antigenic. One of skill in the art would have been motivated to produce the immunogen as combined because Stuart et al, 1987 teach that GLXA polysaccharide is antigenic and suggest that it is reasonable to assume that soluble antigens may play a role in the immunopathology associated with diseases caused by *Chlamydia* (page 533). Additionally, Dick, Jr. et al teach that glycoconjugate vaccines directed against pathogenic bacteria are known in the art. See Table I. Dick, Jr. et al disclose properties of glycoconjugate vaccines as well as design choices that must be taken into consideration when preparing glycoconjugate vaccines. See Tables 2 and 3.

4. Claim 10 is rejected under 35 U.S.C. 103(a) as unpatentable over Whittum-Hudson et al *(Nature Medicine, October 1996, 2(10), 1116-21)* in view of Stuart et al *(Immunology, 1987)* in view of Stuart et al *(Current Microbiology, Vol. 28, 1994, pp. 85-90)* and Dick, Jr. et al *(Conjugate Vaccine, Contrib. Microbiol Immunolo. Basel., Karger 1989, Vol. 10, pp. 48-114)* as applied claims 7, 9 and 18-20 above and further in view of Semprevivo *(Carbohydrate Research, 1988, 177, p. 222-227).*

Claim 10 is drawn to the composition of claim 9, wherein the linker is 2-(4-aminophenyl)ethylamine.

The teachings of Whittum-Hudson, Stuart 1987, and Stuart 1994 and Dick, Jr. et al have been described above.

The combination of Whittum-Hudson et al, Stuart 1987, Stuart, 1994 and Dick, Jr. et al as set forth *supra* does not teach that the linker is 2-(4-aminophenyl)ethylamine.

Semprevivo teaches 2-(4-aminophenyl)ethylamine linkers. Semprevivo teaches that oligosaccharides behave as simple haptens and must be linked either to proteins or a solid support in order to raise and isolate a specific antibody (see the Abstract). Semprevivo teaches that all oligosaccharides regardless of size become associated with the carrier protein (page 225). Semprevivo teaches that coupling oligosaccharides with a 2-(4-aminophenyl)ethylamine linker conserves that chemical integrity of the oligosaccharide.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the 2-(4-aminophenyl)ethylamine linkers as taught by Semprevivo to covalently bond the carrier group (diphtheria toxoid or tetanus toxoid) to the oligosaccharide as taught by the combined art references (Whittum-Hudson et al, Stuart, 1987, Stuart 1994, and Dick, Jr. et al) as combined above because Semprevivo has demonstrated that 2-(4-aminophenyl)ethylamine linkers can be used to form oligosaccharide-protein conjugates (see the Abstract). One would be motivated use of 2-(4-aminophenyl)ethylamine linkers to produce the claimed chlamydial glycolipid-oligosaccharide conjugated of because 2-(4-aminophenyl)ethylamine teach the 2-(4-aminophenyl)ethylamine can be used to couple proteins via their phenylisothiocyanate intermediates under conditions that preserve labile sugar linkages (see the Abstract). Additionally, Dick, Jr. et al teach that

carbohydrate components can be covalently linked to carrier proteins to enhance the immune response to the response to carbohydrate component. Dick, Jr. et al also teach that glycoconjugate vaccines directed against pathogenic bacteria are known in the art. See Table I. Dick, Jr. et al disclose properties of glycoconjugate vaccines as well as design choices that must be taken into consideration when preparing glycoconjugate vaccines. See Tables 2 and 3.

5. Claim 10 is rejected under 35 U.S.C. 103(a) as unpatentable over Whittum-Hudson et al *(Nature Medicine, October 1996, 2(10), 1116-21)* in view of Stuart et al (Immunology, 1987) in view of Stuart *(Current Microbiology, Vol. 28, 1994, pp. 85-90)* and Dick, Jr. et al *(Conjugate Vaccine, Contrib. Microbiol Immunolo. Basel., Karger 1989, Vol. 10, pp. 48-114)* as applied claims 7, 9 and 18-20 above and further in view of Smith et al (*Journal of Biological Chemistry, 255(1), 1980, p. 55-59*).

Claim 10 is drawn to the composition of claim 9, wherein the linker is 2-(4-aminophenyl)ethylamine.

The teachings of Whittum-Hudson, Stuart 1987, and Stuart 1994 and Dick, Jr. et al have been described above.

The combination of Whittum-Hudson et al, Stuart 1987, Stuart, 1994 and Dick, Jr. et al as set forth *supra* does not teach that the linker is 2-(4-aminophenyl)ethylamine.

Smith et al teach the β-(p-aminophenyl)ethylamide (i.e. 2-(4-aminophenyl)ethylamine) can be used to couple proteins via their phenylisothiocyanate

intermediates under conditions that preserve labile sugar linkages (see the Abstract). Smith et al teach the coupling of oligosaccharides to bovine serum albumin and keyhole limpet hemocyanin (see the Abstract). Smith et al teach that rabbits immunized with the synthetic glycoproteins produced antibodies directed against the oligosaccharides (see the Abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the β-(p-aminophenyl)ethylamide (i.e. 2-(4-aminophenyl)ethylamine) linkers as taught by Smith et al to covalently bond the carrier group (diphtheria toxoid or tetanus toxoid) to the oligosaccharide as taught by the prior art (Whittum-Hudson et al, Stuart, 1987, Stuart, 1994 and Dick, Jr. et al) as combined above because Smith et al have demonstrated that β-(p-aminophenyl)ethylamide linkers can be used to form oligosaccharide-protein conjugates (see the Abstract). One would be motivated use of β-(p-aminophenyl)ethylamine linkers to produce the claimed chlamydial glycolipid-oligosaccharide conjugated of because Smith et al teach the β-(p-aminophenyl)ethylamide (i.e. 2-(4-aminophenyl)ethylamine) can be used to couple proteins via their phenylisothiocyanate intermediates under conditions that preserve labile sugar linkages (see the Abstract). Additionally, Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins to enhance the immune response to the response to carbohydrate component. Dick, Jr. et al also teach that glycoconjugate vaccines directed against pathogenic bacteria are known in the art. See Table I. Dick, Jr. et al disclose properties of glycoconjugate vaccines as

well as design choices that must be taken into consideration when preparing glycoconjugate vaccines. See Tables 2 and 3.

Status of Claims

6. No claims are allowed.

Conclusion

7. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
February 28, 2006

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PRIMARY EXAMINER